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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/115,589	07/15/1998	JENNIFER E. VAN EYK	12917	1553

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LICATLA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
GUCKER, STEPHEN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/115,589	VAN EYK ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-98* is/are pending in the application.

4a) Of the above claim(s) *67 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-66,68-69,71-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

3. Newly submitted claims 56-98 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: Applicant's election filed 3/10/00 limits the instant claims to methods employing antibodies and functional fragments thereof and excludes as non-elected non-antibody proteins and fragments thereof and peptidomimetics. Therefore, the instant claims are only being examined to the extent that they read on methods employing antibodies and functional fragments thereof. Applicant's election filed 3/10/00 limits the instant claims to methods employing troponin I and residues 1-193 of troponin I (SEQ ID NO:21) and excludes as non-elected troponin T, troponin C, α-actinin, and SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, and SEQ ID NO:33. Therefore, the instant claims are only being examined to the extent that they read on methods employing troponin I and residues 1-193 of troponin I (SEQ ID NO:21). Applicant's election filed 3/10/00 limits the instant claims to methods employing a myosin light chain 1 peptide fragment comprising residues 20-199, which almost corresponds to SEQ ID NO:28 (see new matter rejection below), and excludes other myosin light chain 1 peptide fragments such as SEQ ID NO:29. Therefore, the instant claims are only being examined to the extent that they

read on methods employing myosin light chain I and residues 20-199 of myosin light chain I (almost SEQ ID NO:28). Applicant's election filed 12/13/01 limits the instant claims to methods of assessing muscle damage by assessing modification of peptide fragments of tropinin I and excludes as non-elected peptide fragments of α-actinin, troponin C, and myosin light chain I. Therefore, the instant claims are only being examined to the extent that they read on modified peptide fragments of tropinin I.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 67 and 70 are completely withdrawn from consideration as being directed to a non-elected invention, and claims 56-66, 68-69, and 71-98 are only being examined to the extent outlined above. See 37 CFR 1.142(b) and MPEP § 821.03.

4. The amendment filed 8/6/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: paragraphs beginning at page 9, line 21, page 29, line 4, and page 32, line 19: epitope TnI amino acid residues 188-199 have been replaced by residues 137-148 (SEQ ID NO:47). No explanation is provided as to why the residue numbering has changed. In the paragraph beginning at page 10, line 21: a myofilament protein modification product can be a peptide fragment of myosin light chain 1, such as all or a portion of all the carboxyl-terminal region consisting of amino acids 20 to 199 has been changed to amino acids 20 to 192 (SEQ

ID NO:28). No explanation is given for the shortening of the amino acid sequence. Same alteration is made of the myosin light chain 1 fragment sequence in paragraph beginning on page 12, line 14, paragraph beginning on page 14, line 3, paragraph beginning on page 24, line 12, and paragraph beginning at page 25, line 4.

Applicant is required to cancel the new matter in the reply to this Office Action.

5. Claims 69 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. SEQ ID NO:28 is a new amino acid sequence as explained above. This is a new matter rejection.

6. Claims 56-59, 71-84, 94, and 96-98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims recite a method of assessing muscle damage in a subject, comprising detecting..." without a recitation of the specific process steps taken in order to do the detecting. Without a recitation of the specific process steps involved in the detecting, the metes and bounds of the claims are indefinite because it cannot be determined what is specifically encompassed by the method of detection, i.e. an act of mental computation, a sensory determination based on visual inspection, smell, or taste, a process that uses scientific reagents and/or equipment, etc.

7. Claims 56-65, 68-69, 71-90, and 92-98 are rejected under 35 U.S.C. 102(b) as being anticipated by Löfberg et al. ("Löfberg") for reasons of record and the following. Löfberg discloses the use of various antibodies and detectable labels and markers (iodine-125, antibodies conjugated to solid-phase magnetic particles, and immunoenzymometric assays, page 1211) to detect two different fragments of myosin heavy-chain, troponin I, and troponin T for the purpose of assaying acute muscle damage, irreversible cardiac and skeletal muscle damage, and reversible cardiac and skeletal muscle damage from biological samples such as serum (pages 1211-1212). When an antibody binds to two different myosin heavy chain fragments and troponin protein as it does in the Löfberg reference, it meets the limitations of a "a peptide fragment of a myofilament protein and an intact protein" because the intact protein is the antibody and a peptide fragment of a myofilament protein includes "all or a portion of a cardiac tropinin I peptide fragment", limited for the purposes of this examination to SEQ ID NO:21. A portion of a peptide fragment has no lower limit; it could be a single or a few amino acids. The proteins used by Löfberg meet the limitations of a portion of SEQ ID NO:21 because they share multiple stretches of amino acid identity that meet the definition of portion of a cardiac troponin I peptide fragment. Löfberg meets all the claim limitations, including assaying serum for different fragments or epitopes from myosin heavy-chain (same protein), and comparing such with serum levels of troponin T and troponin C (different proteins, page 1212) and measuring amounts over time and constructing ratios (page 1213 and Figures 1 and 2) to indicate the extent of muscle

damage (how long the damage lasted over time, whether it involved skeletal muscle, cardiac muscle, or both, etc.).

8. Claims 56-65, 68-69, 71-90, and 92-98 are rejected under 35 U.S.C. 102(b) as being anticipated by Westfall et al. ("Westfall") for reasons of record and the following. Westfall discloses the use of various antibodies and detectable markers (alkaline phosphatase, page 303) to detect fragments from both troponin I and troponin T (abstract) for the purpose of assaying cardiac muscle damage from ischemia from biological samples such as a component of cardiac muscle tissue (page 303). The amount of damage is correlated with time of ischemia (30 minutes as compared to 60 minutes) and ratios were established between the gradual reduction of whole troponins and the appearance of troponin fragments (pages 307-308, Figures 10 and 11, and Table 1). When an antibody binds to two different troponin fragments (such as from troponin I and troponin T) as it does in the Westfall reference, it meets the limitations of a "a peptide fragment of a myofilament protein and an intact protein" because the intact protein is the antibody and a peptide fragment of a myofilament protein includes "all or a portion of a cardiac tropinin I peptide fragment", limited for the purposes of this examination to SEQ ID NO:21. A portion of a peptide fragment has no lower limit; it could be a single or a few amino acids. The proteins used by Westfall meet the limitations of a portion of SEQ ID NO:21 because they share multiple stretches of amino acid identity that meet the definition of portion of a cardiac troponin I peptide fragment.

9. Claims 56-66, 68-69, and 71-98 are rejected under 35 U.S.C. 102(b) as being anticipated by Wicks et al. (WO 94/27156, "Wicks") for reasons of record and the

following. Wicks discloses the use of antibodies and detectable labels and markers (enzymes, alkaline phosphatase, page 12) to detect troponin I (and specific fragments claimed, page 5 and claims 12-13, 18, 26-27, 32-34, and 36) and troponin C in a complex in sandwich assays having immobilized solid phases for the purpose of assaying irreversible cardiac damage from biological samples such as blood (pages 2-5). When an antibody binds to two different troponin fragments (such as from troponin I and troponin C) as it does in the Wicks reference, it meets the limitations of a "a peptide fragment of a myofilament protein and an intact protein" because the intact protein is the antibody and a peptide fragment of a myofilament protein includes "all or a portion of a cardiac tropinin I peptide fragment", limited for the purposes of this examination to SEQ ID NO:21. A portion of a peptide fragment has no lower limit; it could be a single or a few amino acids. The proteins used by Wicks meet the limitations of a portion of SEQ ID NO:21 because they share multiple stretches of amino acid identity that meet the definition of portion of a cardiac troponin I peptide fragment.

10. Claims 56, 60-66, 68-69, and 71-79 are rejected under 35 U.S.C. 102(b) as being anticipated by Takahashi et al. (WO 96/10078, "Takahashi") for reasons of record and the following. Takahashi discloses the use of antibodies and detectable labels and markers (enzymes, peroxidase and alkaline phosphatase, pages 6-7 and 9) to detect myosin light chain 1 (MLC-1) in a complex in sandwich assays having immobilized solid phases (pages 10 and 12) for the purpose of assaying cardiac damage from biological samples such as blood (pages 2-5). When an antibody binds to MLC-1 as it does in the Takahashi reference, it meets the limitations of a "a peptide fragment of a myofilament

protein and an intact protein" because the intact protein is the antibody and a peptide fragment of a myofilament protein includes "all or a portion of a cardiac tropinin I peptide fragment", limited for the purposes of this examination to SEQ ID NO:21. A portion of a peptide fragment has no lower limit; it could be a single or a few amino acids. The proteins used by Takahashi meet the limitations of a portion of SEQ ID NO:21 because they share multiple stretches of amino acid identity that meet the definition of portion of a cardiac troponin I peptide fragment.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961. The fax phone number for this Group is currently (571) 273-8300.

SG

Stephen Gucker

January 10, 2005

Brenda Brumback

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600